

IRRITABLE BOWEL SYNDROME

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What is the Irritable Bowel Syndrome?

The irritable bowel syndrome (IBS) is a disorder of bowel *function* (as opposed to being due to an anatomic abnormality). Patients who suffer from irritable bowel syndrome have changes in bowel habits such as constipation or diarrhea, and abdominal pain along with other symptoms including abdominal bloating, and rectal urgency with diarrhea. In addition, irritable bowel syndrome may be associated with a number of non-intestinal (“extraintestinal symptoms”), such as difficulty with sexual function (pain on intercourse or lack of libido), muscle aches and pains, fatigue, fibromyalgia syndrome, headaches, back pain, and sometimes urinary symptoms including urinary urgency, urinary hesitation or a feeling of spasm in the bladder.

IBS is an extremely common disorder. Studies have estimated the prevalence in the United States is somewhere between 15% and 20% of the entire population. IBS is seen in similar frequencies in other countries around the world. Most studies suggest that irritable bowel syndrome is more common in women with almost twice as many women having the disorder compared to men. The reason why women are more commonly affected by irritable bowel syndrome is not completely understood. It does not seem to be merely due to hormonal differences between men and women. Rather it seems to be due to differences in how women and men process sensations from the intestines, both in the intestinal nervous system (“enteric nervous system”) as well as the brain and spinal cord (“central nervous system”). The frequency of IBS seems to be the same across racial, ethnic and national boundaries.

Despite the fact that irritable bowel syndrome is so common, most people with IBS do not see a doctor for their symptoms. It is estimated that only 1 in 4 people with IBS see a doctor (and thus become a patient with IBS). Reasons why some people chose to see a doctor and others do not are not completely understood. Interestingly severity of gastrointestinal symptoms from IBS alone does not seem to be the major driving factor. Rather the impact of IBS on the patient’s ability to function on a day-to-day basis while having IBS symptoms, the stress from having IBS, and concerns about other diseases that they might have are some of the more frequent reasons patients see their doctor for IBS like symptoms.

Irritable bowel syndrome is not associated with serious medical consequences. People with IBS tend to live long, and in some studies, somewhat longer than individuals who do not have IBS. IBS is not associated with other serious GI diseases, such as inflammatory bowel disease (Crohn’s disease or ulcerative colitis) or colon cancer. The presence of IBS does not put extra stress on the other organs in the body such as the heart, liver or



kidneys. Overall the prognosis for irritable bowel syndrome is excellent. Patients suffering from IBS should not be worried about it leading to other serious diseases. The major problem with IBS is not because it causes death or serious disease, but because it changes the quality of life for the patient. In the last 20 years, we have come to understand how important quality of life is for patients suffering from health problems (called 'health related quality of life', HRQOL for short). We now understand that severity of all diseases, not just IBS, cannot be measured only with tests or how severe symptoms are. Rather we have begun to understand that the true measure of the impact of any disorder is the negative impact on a patient's HRQOL. In IBS, health related quality of life is usually poor, and therefore IBS is a particularly troublesome disease. Studies have shown that when compared to patients with no medical problems, patients with diabetes, gastro esophageal reflux disease (GERD), as well as individuals who have no gastro intestinal disorders, patients with IBS had significantly higher degrees of impairment in their quality of life. By this is meant their physical functioning, their ability to participate in the activities of daily living, their level of emotional distress, their sexual functioning and all the other components that go into a happy and healthy normal life without disease. This is the true impact of IBS and is an important reason that it deserves serious attention from the medical community. IBS is also a costly disease, not only in terms of money spent for health care but also money lost because patients cannot work while they have symptoms. It is estimated that IBS patients because of their inability to participate in work activities, school activities, etc. lose \$30 to \$90 billion per year in productivity. After the common cold, IBS is the second most frequent reason people take days off from work in the United States. This makes IBS a very important issue for public health and the society in general, which clearly needs to be addressed by the medical community.

What Causes Irritable Bowel Syndrome?

The exact cause of irritable bowel syndrome is not known. However, tremendous advances in our understanding of this common and disabling disorder have been made in the last 10 years. Abnormal motility in terms of the bowel moving too fast (which causes diarrhea) or too slow (which causes constipation) is certainly part of this syndrome. However, this represents only one part of a complicated disease. The symptoms of pain, incomplete emptying of the bowels, and bloating cannot be blamed only on abnormal GI motility. Over the last 20 years a number of very well done scientific studies have demonstrated that individuals with IBS tend to have higher levels of sensitivity in the intestines compared to individuals who do not have IBS.

In the last 10 years, we found and identified certain chemicals present in the intestines, which send signals from nerve endings from the intestines to the brain, and also from the brain to the intestines. These chemicals are called "neuro transmitters" and work as messengers between nerve endings to carry signals in both directions between the brain and gut. This is very important because it has led to the development of new drugs. Some of these drugs are currently available. Others are being developed, as we better understand how these chemical 'neurotransmitters' work. One of the major neuro



transmitters involved in sensation of pain in the gut as well as playing a key role in motility activity of the gut is serotonin. This chemical also known by its chemical abbreviation 5-HT. However, serotonin is only one of a large number of neuro transmitters that are present in the gut. As we identify more and more of these substances and better understand their actions, we may be able to further supplement the arsenal of medications that will influence these neuro transmitters and thus help relieve the symptoms of IBS. Clearly the future is quite bright both for better understanding this perplexing and disabling disorder as well as using this knowledge to make newer and better treatments for IBS.

How is Irritable Bowel Syndrome Diagnosed?

Irritable bowel syndrome has several symptoms. A number of IBS experts have met over the last 15 years in Rome, Italy to decide which symptoms would help doctors to make the diagnosis of IBS and other similar diseases as well as to discuss the best methods to diagnose and treat these diseases. The “Rome Diagnostic Criteria” that these experts recommended say that a patient must have symptoms consistent with IBS for at least 3 months over the previous year before this diagnosis can be considered. Altered bowel habits and the presence of lower abdominal pain is key to making a diagnosis of IBS. There are other parts to the Rome Criteria and these can be obtained from your physician. Your doctor can use the Rome Criteria to make a diagnosis of IBS. However, taking a careful medical history is essential to identifying IBS, and identifying and addressing through treatment the specific symptom complaints of the patient is a key component. Should your doctor in the course of his/ her history taking, physical examination discover findings which are of concern he or she will order additional tests to make sure you do not have other gastro intestinal disorders. Should nothing emerge during your doctor visit from the history, physical examination and from routine blood studies that are commonly performed during an office visit for IBS-like symptoms your doctor will most likely make an IBS diagnosis. The safety and accuracy of making an IBS diagnosis based on the Rome II criteria has been the subject of a number of studies which have confirmed these criteria as accurate and correct in making a diagnosis of IBS anywhere from 65% to 100% of the time, again with strong reliance on the patient’s symptoms. In most cases endoscopy (looking at the lining of the stomach and upper intestines and/or colon by the use of an endoscope, a long tube with a video camera at the tip) is not necessary for the diagnosis of IBS. There are a number of situations where endoscopy may be performed. The first is that everyone should be screened for colon cancer according to standard guidelines. Anyone age 50 or older who has IBS-like symptoms should have a colonoscopy as part of a routine screening examination to rule out colon cancer. For people who have a family history of colon cancer in a parent, brother or sister the recommended age for screening colonoscopy is 40 years old. Likewise, your doctor may perform upper endoscopy if you have certain symptoms like persistent diarrhea that does not sound like IBS. Your doctor may also order other tests like a CAT scan of the abdomen (a special x-ray of the abdomen which shows the organs in the abdomen particularly the pancreas, gall bladder and liver as well as the intestines) or certain blood tests. Surgery is rarely required for the diagnosis of IBS and should be avoided.



Sometimes patients are willing to undergo surgery because their pain is so severe. Studies have shown that surgery done only for an indication of IBS-like pain is usually not helpful in finding the cause of the patient's pain or leading to improvement in the patient's pain symptoms.

How is IBS Treated?

In past years IBS was treated from the perspective that it was a "motility disorder". The use of fiber supplementation to improve intestinal motility or movement was a common recommendation. While some studies have questioned whether fiber supplementation alone is helpful for the treatment of IBS and its symptoms, there are other good reasons to consume a high fiber diet. High fiber diets are associated with lower blood sugar, lower cholesterol as well as a lower tendency to form diverticula or outpouchings of the colon. Moreover, some patients with IBS report having a good result with a high fiber diet. Certainly every patient should include at least 25 grams of fiber in their diet every day. However, should your IBS symptoms not improve with fiber supplementation you should not be disappointed. Other drugs that have been used in the past including antispasmodics and other drugs will decrease GI motility. These drugs have not been shown to be particularly helpful in the treatment of IBS although again some patients will find them helpful. Likewise, laxatives and other drugs can treat the individual symptoms of constipation and diarrhea associated with IBS but will not treat the global symptoms of IBS, including abdominal pain, bloating, rectal urgency which accompanies constipation and diarrhea associated with IBS. Stressful life experiences can worsen IBS symptoms and it is important you seek advice for stress reduction from your primary care clinician if you are having difficulty dealing with the stress.

In the section above on the cause of irritable bowel syndrome, we have discussed the important role of serotonin. A number of new drugs have been developed to increase or decrease the action of serotonin on the intestines, and therefore try to treat IBS symptoms. The first such drug to be available was alosetron (Lotronex®). This drug, which was approved by the FDA for the treatment of IBS with diarrhea in women, works on a specific type of serotonin called 5-HT₃, and so alosetron is referred to as a 5-HT₃ antagonist. This drug blocks the effects of serotonin in intestinal cells and is indicated for the treatment of IBS with diarrhea in women. However, this drug can rarely decrease blood flow to the colon and sometimes cause a potentially serious colon inflammation as a result (ischemic colitis). This condition is associated with low blood flow to the colon. It is usually seen in older patients with heart problems, and why it occurs with alosetron use is not known. Although this colon inflammation usually gets better on its own, it can cause serious problems, and therefore patients taking alosetron need to be carefully monitored. It is also important to recognize that alosetron is a very potent drug; it is intended for patients with serious diarrhea and ought not be used by persons with occasional, modest diarrhea. To add an extra level of caution when using these drugs, the drug company that makes alosetron (GlaxoSmithKline, Inc.) and the Food and Drug Administration (FDA) have developed a special program to monitor patients who take alosetron and also to make sure patients understand the risk associated with the



medication. Information on this program can be obtained from your doctor. The risk of ischemic colitis from Alosetron is approximately 1 in 250 to 1 in 750 patients. Otherwise, alosetron is an extremely effective medicine for the treatment of severe IBS with diarrhea. However, because of the risks associated with the medication it is only given to people with “severe IBS with diarrhea that does not get better with other treatments”.

Another new drug that works on intestinal serotonin is Tegaserod (Zelnorm®). Zelnorm® works on a subtype of serotonin called 5-HT₄. Tegaserod is a selective 5-HT₄ agonist and acts as a pro-motility agent by activating the 5-HT₄ receptors in the nerve processes of the enteric ganglia and smooth muscle cells of the GI tract. Tegaserod increases the action of serotonin on certain intestinal cells, and helps treat constipation in women with IBS. So far, tegaserod appears to be quite safe. Tegaserod has also been linked to a few patients with colon inflammation from low blood flow (ischemic colitis) but at a much much lower rate than that seen with alosetron. Because of this, there is no special program for prescribing tegaserod like there is with alosetron.

In addition to these important advances in drug therapy, a number of other drugs that affect neurotransmitters as well as new drugs looking at serotonergic function are under development. It is clear in the next few years we are likely to see a significant increase in the number of drugs available to treat IBS.

Conclusion

Irritable bowel syndrome is not a trivial illness. It deeply affects the quality of life of the patient and their ability to function effectively in society. The economic cost of irritable bowel syndrome has been estimated to be over \$80 billion a year to the American economy. However, above and beyond this is the large number of people in our society who experience IBS symptoms daily who in the past have suffered because there was no effective treatment available. Patients with IBS should see their physician and get recommendations on the latest treatments available. However, it is also important that the patient with IBS understands that although this is a chronic illness, symptoms can be controlled, and the overall outlook is actually quite good.

